Page 63, after the last line, beginning on a new page, please insert the attached Sequence Listing.

REMARKS

Claims 1-23 are active in this application. Applicants have now submitted a Sequence Listing and a corresponding computer-readable Sequence Listing. Sequence Identifiers (SEQ ID NO:) have been added to the specification. The sequence information recorded in the corresponding computer-readable Sequence Listing is identical to the paper copy of the Sequence Listing. Support for all of the sequences listed in the Sequence Listing is found in the present application as originally filed. No new matter is believed to have been introduced by the submission of the Sequence Listing and the corresponding computer-readable Sequence Listing.

Applicants submit that the present application is now ready for examination on the merits. Early notification of such is earnestly solicited.

Respectfully submitted,

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Marked-Up Copy
Serial No: 09/446,109
Amendment Filed on:
5-3-01

IN THE SPECIFICATION

Please amend the specification as follows:

Page 29, lines 3-20, please replace the paragraph as follows:

--We have focussed on the C-terminal residues of C5a, in order to explore structure-activity relationships in the search for peptide sequences with potent agonist activity. Many of these peptides are full agonists relative to C5a, but have markedly lower potency (Sanderson et al, 1994, 1995; Finch et al, 1997). Our initial structure-activity investigations have been particularly informative. Mutating the decapeptide C-terminus of C5a (SEQ. ID NO:1, $C5a_{65-74}$, ISHKDMQLGR) twice with $I_{65}Y$ and $H_{67}F$ (eg. 2) led to enhancement of agonist potency by about 2 orders of magnitude. These results are summarised in Table 2. Analyses of Ramachandran plots and 2D NMR spectra for compound 2 suggested that certain structural features, namely a twisted "helix-like" backbone conformation for residues 65-69 and a ß-turn for residues 71-74, might be responsible for activity. These preliminary results provided some insight to structural requirements for tight binding to a C5a receptor.--

Pages 30 and 37, please replace Tables 2 and 4 as shown on the attached pages:

--Table 2

Pharmacological Activity of C5a Agonist Analogues*

Peptide No.	Peptide	Fetal Artery EC_{50} (μM)	PMN Enzyme Release EC_{50} (μM)	Binding Affinity IC_{50} (μM)
SEQ. ID NO:1	$C5a_{65-74}$ (ISHKDMQLGR)	>1000	>1000	>1000
SEQ. ID NO:2	YSFKDMQLGR	9.6	92	1.3
SEQ. ID NO:3	YSFKDMPLaR	0.5	72	3.7
SEQ. ID NO:4	YSFKPMPLaR	0.2	4.1	6.0
SEQ. ID NO:5	$C5a_{37-46}$-ahxYSFKPMPLaR	0.06	5.9	0.7
SEQ. ID NO:6	$C5a_{12-20}$-ahxYSFKPMPLaR	0.08	0.7	0.07
	C5a	0.02	0.03	0.0006

*Finch *et al*, 1997

Table 4

Receptor-Binding Affinities[a] and Antagonist Activities[b] in Human PMNs

	Compound	Receptor Affinity[a] IC_{50} (μM)	Antagonist Potency[b] IC_{50} (μM)	Agonist Activity[c]
SEQ. ID NO:7	MeFKP(dCha)Wr	1.8 (15)	0.085 (9)	No
SEQ. ID NO:8	MeFKP(dCha)Wr-$CONH_2$	14 (5)	0.5 (3)	No
SEQ. ID NO:9	MeFKP(dCha)WR	11 (5)	0.7 (3)	No
SEQ. ID NO:10	MeFKPLWR	144 (1)	>1000 (3)	nd
SEQ. ID NO:11	Ac-F-[KP(dCha)Wr]	3.2 (40	0.090 (5)	No
SEQ. ID NO:12	Ac-F-[OP(dCha)Wr]	0.28 (6)	0.012 (4)	No
SEQ. ID NO:4	YSFKPMPLaR	6.0[d]	-	Yes
SEQ. ID NO:1	$C5a_{65-74}$, ISHKDMQLGR	>1000[e]	-	-
	C5a	0.0008 (9)	-	Yes

Number of experiments in parenthesis. Corrected for amino acid content

Square brackets indicate cyclic portion.

nd= not determined

[a] 50% reduction in binding of ^{125}I-C5a to intact human PMNs

[b] 50% reduction in myeloperoxidase secretion from human PMNs mediated by 100 nM C5a

[c] Agonist activity in dose range 0.1 nM-1 nM

[d] Finch *et al*, 1997; [e] Kawai *et al*, 1991

Page 39, please replace the text beginning at line 6 through the end of the page as follows:

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Compound	n	R	Isomer*	Receptor Affinity μM	Agonist Activity
SEQ. ID NO:13	1	H	S-	9	No
SEQ. ID NO:14			R-	34	No
SEQ. ID NO:15	2	H	S-	0.3	No
SEQ. ID NO:16			R-	3.7	No
SEQ. ID NO:17	3	Ac	S-	0.3	No
SEQ. ID NO:11		Ac	R-	38	No
SEQ. ID NO:18	4	Ac	S-	3.2	No
SEQ. ID NO:12		Ac	R-	51	No

Refers to stereochemistry of Arg side chain --

Pages 41 and 42, please replace Table 6 as shown on the attached page:

--Table 6

Effect of Cyclisation on Antagonist Binding Affinity and Antagonist Potency

	PEPTIDE	$pD_2 \pm SE^a$	IC_{50} (μM)[a]	(n)	$pD_2 \pm SE^b$	IC_{50} (μM)[b]	(n)
SEQ. ID NO:11	AcF-[KPdChaWR]	5.49 ± 0.22	3.2	4	7.07 ± 0.29	0.09	5
SEQ. ID NO:18	AcF-[OPdChaWR]	6.44 ± 0.14*	0.4	9	7.30 ± 0.09	0.05	9
SEQ. ID NO:19	[FWPdChaWR]	4.37 ± 0.36*	43	3	nd		
SEQ. ID NO:20	AcF-[KMdChaWR]	4.81 ± 0.06	15	2	nd		
SEQ. ID NO:21	AcF-[KKdChaWR]	3.94 ± 0.4	116	3	4.88	13	1

Effect of length of linker in cycle on antagonist binding affinity and antagonist potency

SEQ ID NO:22	AcF-[XPdChaWR]	5.02 ± 0.07	9.5	3	4.71 ± 0.23	20	3
SEQ ID NO:23	AcF-[X^2PdChaWR]	4.77 ± 0.14*	17	3	6.09 ± 0.08*	0.8	4
SEQ ID NO:11	AcF-[OPdChaWR]	4.60 ±0.06*	16	4	6.42 ± 0.10	0.4	4
SEQ ID NO:24	AcKF-[OPdChaWR]	4.96 ± 0.03	11	3	6.73	0.2	1

Table 6 (cont.)

	PEPTIDE	$pD_2 \pm Se^a$	IC_{50} (μM)[a]	(n)	$pD_2 \pm SE^b$	IC_{50} (μM)[b]	(n)
SEQ. ID NO:14	F-[XPdChaWR]	4.39 ± 0.10*	41	3	nd		
SEQ. ID NO:16	F-[X^2PdChaWR]	5.42 ± 0.05	3.8	3	6.70 ± 0.04	0.4	3

SEQ. ID NO:25	F-[OPdChaWR]	5.51 ± 0.07	3.1	3	5.79 ± 0.34*	1.6	3
SEQ. ID NO:26	F-[KPdChaWR]	5.09 ± 0.08	8.1	3	5.55 ± 0.57*	2.8	3
Effect of L-Arg on antagonist binding affinity and antagonist potency							
SEQ. ID NO:17	AcF-[OPdChaWR]	6.57 ± 0.05*	0.3	3	7.91 ± 0.17*	0.01	3
SEQ. ID NO:13	F-[XPdChaWR]	4.98 ± 0.05	10	3	5.63 ± 0.13*	2.4	3
SEQ. ID NO:15	F-[X^2PdChaWR]	6.50 ± 0.04*	0.3	5	7.36 ± 0.13	0.04	3
SEQ. ID NO:27	F-[OPdChaWR]	7.21 ± 0.01*	0.06	3	7.41 ± 0.14	0.04	3
SEQ. ID NO:28	F-[KPdChaWR]	6.50 ± 0.12*	0.3	4	6.69 ± 0.04	0.2	3

Page 63, after the last line, beginning on a new page, please insert the attached Sequence Listing.